Workplace exposures and oesophageal cancer

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Abstract

***Objectives*—To describe the relation between oesophageal cancer and many occupational circumstances with data from a population based case-control study.**

***Methods*—Cases were 99 histologically confirmed incident cases of cancer of the oesophagus, 63 of which were squamous cell carcinomas. Various control groups were available; for the present analysis a group was used that comprised 533 population controls and 533 patients with other types of cancer. Detailed job histories were elicited from all subjects and were translated by a team of chemists and hygienists for evidence of exposure to 294 occupational agents. Based on preliminary results and a review of literature, a set of 35 occupational agents and 19 occupations and industry titles were selected for this analysis. Logistic regression analyses were adjusted for age, birthplace, education, respondent (self or proxy), smoking, alcohol, and β-carotene intake.**

***Results*—Sulphuric acid and carbon black showed the strongest evidence of an association with oesophageal cancer, particularly squamous cell carcinoma. Other substances showed excess risks, but the evidence was more equivocal—namely chrysotile asbestos, alumina, mineral spirits, toluene, synthetic adhesives, other paints and varnishes, iron compounds, and mild steel dust. There was considerable overlap in occupational exposure patterns and results for some of these substances may be mutually confounded. None of the occupations or industry titles showed a clear excess risk; the strongest hints were for warehouse workers, food services workers, and workers from the miscellaneous food industry.**

***Conclusions*—The data provide some support for an association between oesophageal cancer and a handful of occupational exposures, particularly sulphuric acid and carbon black. Many of the associations found have never been examined before and warrant further investigation.**

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One of the most intriguing aspects of the epidemiology of oesophageal cancer is its considerable geographical variation. In most developed countries, the incidence is <5/100 000.[1] However certain areas of the world have rates which are several orders of magnitude higher, with particularly high rates seen in northern China, in central Asia around Kazakhstan, and in the Transkei region of Africa.[2] Despite these major geographical clues, the aetiology of oesophageal cancer remains obscure. In developed countries the main risk factors identified to date are heavy alcohol and tobacco use, and low intake of fruit and vegetables or β-carotene.[3–10]

The occupations which have been most consistently linked with the development of oesophageal cancer are work in a brewery[5] and work as a waiter or in a restaurant.[11 12] It is likely that subjects in these occupations have higher exposure to alcohol and cigarette smoke than the general population. Although a wide range of other occupations have been reported to have increased risks in some studies, the findings have often been based on small numbers, the authors have rarely been able to control for confounding by alcohol and tobacco use, and the results have not been repeated in other studies.

In the 1980s, we carried out a large case-control study of multiple cancer sites and hundreds of occupational exposures.[13] A new method of assessing exposure to substances on a case-by-case basis was developed to minimise misclassification of exposure status.[14] The study was initially set up as a hypothesis generating study as many of the exposures had not previously been examined. In this paper, we present a detailed analysis for oesophageal cancer in relation to selected substances, occupations, and industries.

Methods

The design and data collection methods of the population based, case-control study of occupational exposures and cancer have been described previously[15 16] and will be summarised here. Subjects were men resident in the Montreal area, aged 35–70, with a new histologically confirmed cancer at one of 19 anatomical sites. Participation of all large hospitals in the area ensured virtually complete (97%) population based ascertainment of cases. This study was approved by the ethics committees in each hospital, and subjects gave their written, informed consent. There were 4576 eligible patients with cancer between 1979 and 1985, and 3730 of these (82%) were successfully interviewed. Interview responses were obtained from 99 cases of oesophageal cancer (75% response rate), of which 63 were squamous cell carcinoma, 23 were adenocarcinoma, and 13 were of uncertain morphology. Concomitantly, 533 population controls, frequency matched on age, selected from electoral lists by random digit dialling, were interviewed (71% response rate). Eighty one per cent of

Table 1 Criteria for defining exposure groups for each substance, Montreal, 1979–85

*Exposure group**	*Confidence*	*Years since first exposure*	*Concentration × frequency†*	*Duration (y)*
Excluded	Possible	Any	Any	Any
Excluded	Any	≤5	Any	Any
Unexposed	—	—	—	None
Non-substantial	Probable or definite	>5	<4	Any
Non-substantial	Probable or definite	>5	≥4	≤5
Substantial	Probable or definite	>5	≥4	>5

*For each exposure group, all criteria listed on each row must be fulfilled.
†Concentration and frequency are scored as follows: 1=low; 2=medium; 3=high.

subjects responded for themselves; proxies provided information for the rest.

EXPOSURE ASSESSMENT

The questionnaire was in two parts: a structured section requesting information on important cancer risk factors, including age, birthplace, educational level, smoking, and alcohol habits, and frequency of use of some fruit and vegetables, and a semistructured section designed to obtain a detailed description of each job the subject had held in his working lifetime. Occupations were coded according to the seven digit Canadian classification and dictionary of occupations,[17] and industries were coded according to the three digit standard industrial classification manual.[18] For each job in each subject's history, he was asked about the company, its products, the nature of the worksite, his main and subsidiary tasks, and any additional information (equipment maintenance, use of protective equipment, activities of coworkers) that could furnish clues about possible exposures. Interviewers were specially trained and monitored for the occupational interview. For some occupations, supplementary questionnaires were developed and used to assist the interviewers with detailed technical probing.

A team of chemists and industrial hygienists examined each completed questionnaire and translated each job into a list of potential exposures by means of a checklist form that included some 294 substances. This type of retrospective exposure assessment had not been done previously in a community based study, and it took several years to develop a satisfactory method, based on indirect and imperfect information sources. The team of coders, comprising chemists and industrial hygienists, spent about 10 years, or 40 person-years, on this project, including helping to develop the method, helping to monitor the quality of the interviewing, doing background research on exposures in different occupations, coding the files, and recoding after the first round of coding was completed. As sources of information for coding, they used an eclectic, wide ranging, and cumulative information bank, derived, among others, from the following sources: the interviews themselves, which provided a range of quality of information; books, journal articles, and other reports in such diverse fields as industrial engineering, chemistry, and industrial hygiene; and consultants, in particular those who had familiarity with specific industries in the Montreal area. The final codes given to a file were based on consensus among the coders. The chemical coding activity was carried out completely blind to the subject's disease status.

For each product thought to be present in each job, the coders noted three dimensions of information, each on a three point scale: their degree of confidence that the exposure had actually occurred (possible, probable, definite); the frequency of exposure in a normal working week (<5%, 5–30%, >30% of the time); and the relative concentration of the agent to which the worker was exposed (low, medium, or high). Given the retrospective nature of the coding, we did not think that it was possible to attribute more precise quantitative values to the levels of exposure. No exposure was not interpreted as absolute zero; rather, it was considered as exposure up to the level that can be found in the general environment, and to which all subjects may be exposed. Although a subject's job title was certainly a factor in attributing exposure, the details of the subject's activities were taken into account and there were many examples of subjects with the same job title having different exposure profiles, and conversely, many subjects with different job titles were attributed similar exposures.

There were 294 substances in our study and 175 occupation and industry categories. The present analysis was restricted to 30 substances for which there were ≥15 exposed cases of oesophageal cancer; four other substances (carbon black, chromium VI compounds, cellulose, polycyclic aromatic hydrocarbons (PAHs) from coal), which showed increased risks in our screening analyses[15] and for which there were at least 10 exposed cases; and formaldehyde, which has been associated with oesophageal cancer in a previous study.[19]

Table 2 Selected characteristics of case and control groups, Montreal, 1979–85

Characteristic	*Oesophageal cancer cases (n=99)*	*Population controls (n=533)*	*Cancer controls (n=2299)*	*Pooled controls* (n=1066)*
Mean age (y)	59.6	59.6	58.6	59.2
Educational level (%):				
0–6 y	25.3	20.3	22.5	22.2
7–12 y	60.6	56.1	55.2	55.6
≥13 y	14.1	23.6	22.3	22.1
Birthplace (%):				
Québec province	76.2	74.0	70.2	73.1
Rest of Canada, USA	7.1	6.6	7.8	6.1
Southern Europe	7.1	9.4	9.0	9.9
Northern Europe	6.1	6.0	9.4	7.3
Asia, Africa	1.0	3.0	2.3	2.4
Other	2.0	1.1	1.3	1.0
Respondent (%):				
Self	67.7	87.4	80.5	84.1
Proxy	32.3	12.6	19.5	15.9
Beer consumption (%):				
None or social	37.4	70.9	64.7	67.8
Medium	31.3	23.6	25.5	24.8
Heavy	31.3	5.4	9.8	7.4
Spirits consumption (%):				
None or social	66.7	85.2	79.6	81.6
Medium	17.2	11.6	13.6	13.6
Heavy	16.2	3.2	6.9	4.8
β-Carotene index (%):				
Low	55.6	31.3	47.8	40.1
Medium	27.3	36.4	25.8	30.6
High	17.2	32.3	26.4	29.4
Mean cigarette-years	1213	802	845	807
Smoking patterns (%):				
Never smokers	7.1	19.7	17.2	18.9
Stopped ≥11 y	17.2	19.9	23.1	19.9
Stopped 3–10 y	11.1	14.8	11.6	12.9
Current smokers and stopped ≤2 y	64.6	45.6	48.2	48.3

*This group includes the 533 population controls plus 533 selected at random from among the cancer controls.

Table 3 List of substances included in the present analysis and most common occupations in which these substances were coded in the entire study population, Montreal, 1979–85

Substances	*Lifetime prevalence of exposure (%)**	*Main occupations*
Dusts:		
Carbon black	5	Painters and paperhangers; printing press workers; motor vehicle mechanics and repairers.
Chrysotile asbestos	17	Motor vehicle mechanics; welders and flame cutters; stationary engineers.
Alumina	15	Metal machinists; motor vehicle mechanics; carpenters.
Abrasives dust	24	Metal machinists; carpenters; motor vehicle mechanics.
Cellulose	7	Material handlers; printing press workers; shipping and receiving clerks.
Wood dust	23	Carpenters; cabinet and wood furniture makers; other construction workers.
Crystalline silica	24	Carpenters; construction laborers; cabinet and wood furniture makers.
Liquids and vapours:		
Mineral spirits (with benzene, toluene, xylene)	16	Motor vehicle repairmen; painters; stationary engineers.
Toluene	14	Motor vehicle mechanics; motor vehicle refinishers; carpenters.
Synthetic adhesives	15	Shoemakers; carpenters; cabinet and wood furniture makers.
Other paints and varnishes	13	Painters; carpenters; janitors.
Sulphuric acid	9	Motor vehicle mechanics; sheet metal workers; tool and die makers.
Solvents	40	Motor vehicle mechanics; painters; metal machinists.
Lubricating oils and greases	31	Motor vehicle repairmen; machinists; farmers.
Gases and fumes:		
Metal oxide fumes	19	Welders and flame cutters; pipefitters and plumbers; motor vehicle mechanics.
Nitrogen oxides	22	Welders and flame cutters; motor vehicle mechanics; pipefitters and plumbers.
Gasoline engine emissions	42	Truck, taxi and car drivers; motor vehicle mechanics; woodcutters.
Carbon monoxide	50	Motor vehicle drivers; motor vehicle mechanics and repairmen; welders and flame cutters.
Metals:		
Aluminium compounds	19	Metal machinists; carpenters; welders and flame cutters.
Iron compounds	25	Metal machinists; welders and flame cutters; motor vehicle mechanics.
Lead compounds	47	Motor vehicle drivers and driver-salesmen; motor vehicle mechanics; painters.
Chromium (VI) compounds	10	Painters and paperhangers; welders and flame cutters; motor vehicle mechanics and repairers.
Metallic dust	28	Metal machinists; motor vehicle mechanics; welders and flame cutters.
Mild steel dust	17	Metal machinists; welders and flame cutters; motor vehicle mechanics.
Aromatic hydrocarbons:		
PAHs from any source	64	Motor vehicle drivers and salesmen; motor vehicle repairmen; machinists.
Benzo(a)pyrene	22	Motor vehicle mechanics; machinists; foundry workers.
PAHs from coal	8	Stationary engineers and boiler room workers; railway trackmen; pipefitters and plumbers.
PAHs from petroleum	62	Motor vehicle drivers and salesmen; motor vehicle repairmen; machinists.
PAHs from sources other than coal, wood, or petroleum	20	Welders and flame cutters; roofers; chefs and cooks.
Mononuclear aromatic hydrocarbons	34	Motor vehicle mechanics; metal machinists; painters.
Other:		
Aliphatic aldehydes	17	Chefs and cooks; carpenters; textile workers.
Formaldehyde	15	Carpenters; textile workers.
Alkanes (C_5–C_{17})	36	Motor vehicle mechanics; painters; carpenters.
Alkanes (C_{18+})	35	Motor vehicle mechanics; metal machinists; business and industrial machine mechanics.
Cleaning agents	16	Janitors; chefs and cooks; restaurant busboys.

*Prevalence among all 4263 subjects interviewed in our study.
PAHs=polycyclic aromatic hydrocarbons.

Occupations and industries selected for analyses were those with at least 10 exposed cases in our data set, or those suspected as possible risk factors, provided that there were at least four exposed cases.

STATISTICAL ANALYSES

A separate series of analyses was carried out with each of three sets of controls: the 533 population controls; 2299 cancer patients with other types of cancer (excluding patients with cancer of the lung or the stomach); and a pooled group of 1066 controls consisting of the 533 population controls plus an equal number selected at random from among the cancer controls. The following cancer sites were represented in the pooled controls (numbers in parentheses): colorectum (136), prostate (105), bladder (99), lymphoproliferative (58), kidney (46), pancreas (31), melanoma (30), liver (nine), sarcomas (nine), testis (five), gall bladder (three), and other (two).

Unconditional logistic regression was used to model the risk of developing oesophageal cancer with each of the three control groups.[20] All oesophageal cancers were analysed as a group and squamous cell carcinomas were analysed separately.

Substances were incorporated as categorical variables on a three point scale (unexposed, any exposure, and substantial exposure) as described in table 1. We excluded from the analyses those subjects with only possible exposure and those who had been exposed only in the 5 years before diagnosis of their cancer or before the interview.

Occupations and industries were analysed by the number of years of employment, excluding the period of 5 years preceding the diagnosis or enrolment in the study. The unexposed groups comprised subjects who had had never held the occupation or been employed in the industry of interest.

The following variables were entered into the regression models as possible confounders: age (years), responder (self, proxy), education (three levels), birthplace (Montreal, rest of Quebec province, rest of Canada or USA, southern Europe, northern Europe, Asia or Africa, other), beer drinking (none or social, medium, heavy), spirits drinking (none or social, medium, heavy), cumulative amount of cigarettes smoked (natural logarithm of the number of cigarette-years), smoking patterns (never smokers, ex-smokers for at least 11 years, ex-smokers for 3–10 years, ex-smokers for $\leqslant$2 years and current smokers), and an index of β-carotene intake (three levels). This cumulative index was obtained by converting the frequency of use of carrots, spinach,

Table 4 Adjusted OR (95% CI) between oesophageal cancer and exposure to selected occupational substances, by histological subtypes, Montreal, 1979–85*

Substances	Exposure level	All histological subtypes (n=99)			Squamous cell carcinoma (n=63)		
		n_{exp}	OR	95% CI	n_{exp}	OR	95% CI
Dusts:							
Carbon black	Any	11	2.1	1.0 to 4.3	10	3.4	1.5 to 7.7
	Non-substantial	9	1.8	0.8 to 4.0	8	2.9	1.2 to 7.2
	Substantial	2	5.7	0.9 to 36.0	2	8.9	1.2 to 64.3
Chrysotile asbestos	Any	21	1.4	0.8 to 2.4	17	2.0	1.1 to 3.8
	Non-substantial	19	1.4	0.8 to 2.5	16	2.1	1.1 to 4.0
	Substantial	2	1.3	0.3 to 6.2	1	1.1	0.1 to 9.7
Alumina	Any	17	1.3	0.7 to 2.3	14	1.8	0.9 to 3.5
	Non-substantial	14	1.2	0.6 to 2.3	11	1.5	0.7 to 3.2
	Substantial	3	1.6	0.4 to 6.2	3	3.5	0.9 to 13.9
Abrasive dust	Any	22	1.0	0.6 to 1.6	17	1.3	0.7 to 2.3
	Non-substantial	14	1.2	0.6 to 2.3	10	1.5	0.7 to 3.2
	Substantial	8	0.7	0.3 to 1.5	7	1.0	0.4 to 2.5
Cellulose	Any	10	1.5	0.7 to 3.1	4	0.9	0.3 to 2.6
	Non-substantial	8	1.7	0.7 to 4.0	2	1.0	0.3 to 3.7
	Substantial	2	0.9	0.2 to 4.6	2	0.6	0.1 to 4.9
Wood dust	Any	19	0.8	0.4 to 1.3	16	1.0	0.5 to 1.9
Crystalline silica	Any	18	0.7	0.4 to 1.3	13	0.8	0.4 to 1.7
Liquids and vapours:							
Mineral spirits	Any	17	1.1	0.6 to 2.0	16	1.9	1.0 to 3.7
	Non-substantial	8	1.6	0.7 to 3.7	7	2.6	1.0 to 6.6
	Substantial	9	0.9	0.4 to 1.9	9	1.6	0.7 to 3.6
Toluene	Any	16	1.2	0.7 to 2.2	15	2.0	1.0 to 3.9
	Non-substantial	9	1.0	0.5 to 2.2	9	1.8	0.8 to 4.1
	Substantial	7	1.5	0.6 to 3.7	6	2.4	0.9 to 6.4
Synthetic adhesives	Any	19	1.3	0.8 to 2.3	16	1.8	1.0 to 3.4
	Non-substantial	10	1.4	0.7 to 3.0	8	2.0	0.9 to 4.7
	Substantial	9	1.2	0.6 to 2.6	8	1.6	0.7 to 3.8
Other paints and varnishes†	Any	18	1.5	0.8 to 2.6	16	2.3	1.2 to 4.4
	Non-substantial	12	2.0	1.0 to 4.1	10	2.8	1.2 to 6.3
	Substantial	6	1.0	0.4 to 2.4	6	1.8	0.7 to 4.7
Sulphuric acid	Any	15	2.2	1.2 to 4.3	10	2.8	1.2 to 6.1
	Non-substantial	12	2.0	1.0 to 4.0	9	2.2	1.2 to 6.3
	Substantial	3	4.1	1.0 to 17.2	1	3.1	0.3 to 28.1
Solvents	Any	39	1.1	0.7 to 1.7	30	1.4	0.8 to 2.5
	Non-substantial	16	1.0	0.5 to 1.9	12	1.3	0.6 to 2.6
	Substantial	23	1.1	0.6 to 1.9	18	1.6	0.8 to 3.0
Lube oils and greases	Any	25	0.7	0.4 to 1.2	18	0.9	0.5 to 1.6
Gases and fumes:							
Metal oxide fumes	Any	17	1.1	0.6 to 2.0	13	1.5	0.8 to 3.0
	Non-substantial	10	1.5	0.8 to 2.9	7	1.8	0.8 to 4.1
	Substantial	7	0.6	0.2 to 1.8	6	1.1	0.4 to 3.4
Nitrogen oxides	Any	21	0.9	0.6 to 1.6	16	1.2	0.7 to 2.4
Gasoline engine emissions	Any	41	0.9	0.6 to 1.5	24	0.9	0.5 to 1.5
Carbon monoxide	Any	45	0.7	0.4 to 1.1	25	0.6	0.3 to 1.0
Metals:							
Aluminium compounds	Any	19	1.1	0.6 to 1.9	16	1.6	0.8 to 3.0
	Non-substantial	15	1.1	0.6 to 2.1	12	1.5	0.7 to 3.0
	Substantial	4	1.1	0.4 to 3.2	4	2.2	0.7 to 6.8
Iron compounds	Any	25	1.0	0.6 to 1.7	21	1.7	0.9 to 3.0
	Non-substantial	15	1.4	0.7 to 2.6	13	2.3	1.2 to 4.8
	Substantial	10	0.8	0.4 to 1.5	8	1.1	0.5 to 2.6
Lead compounds	Any	41	0.7	0.4 to 1.1	25	0.7	0.4 to 1.3
Chromium VI compounds	Any	6	0.6	0.2 to 1.4	6	1.0	0.4 to 2.6
Metallic dust	Any	27	1.0	0.6 to 1.7	20	1.3	0.7 to 2.3
	Non-substantial	17	1.3	0.7 to 2.3	13	1.7	0.8 to 3.3
	Substantial	10	0.8	0.4 to 1.6	7	0.9	0.4 to 2.2
Mild steel dust	Any	18	1.1	0.6 to 2.0	15	1.7	0.9 to 3.2
	Non-substantial	11	1.3	0.7 to 2.7	10	2.2	1.0 to 4.8
	Substantial	7	0.9	0.4 to 2.0	5	1.1	0.4 to 3.1
Aromatic hydrocarbons:							
PAHs from any source	Any	64	0.9	0.5 to 1.5	40	0.9	0.5 to 1.7
Benzo(a)pyrene	Any	24	1.1	0.7 to 1.9	18	1.6	0.8 to 3.0
	Non-substantial	19	1.0	0.5 to 1.7	16	1.6	0.8 to 3.0
	Substantial	5	2.3	0.8 to 6.5	2	1.7	0.4 to 8.2
PAHs from coal	Any	10	1.2	0.6 to 2.5	5	0.9	0.3 to 2.5
	Non-substantial	4	0.7	0.2 to 2.1	2	0.5	0.1 to 2.4
	Substantial	6	2.0	0.8 to 5.3	3	1.7	0.5 to 6.2
PAHs from petroleum	Any	64	1.0	0.6 to 1.6	41	1.0	0.6 to 1.9
PAHs from other sources	Any	16	0.7	0.4 to 1.2	11	0.7	0.4 to 1.5
Mononuclear aromatic hydrocarbons	Any	29	0.8	0.5 to 1.3	23	1.2	0.7 to 2.0
Other:							
Aliphatic aldehydes	Any	21	1.3	0.8 to 2.4	13	1.2	0.6 to 2.5
	Non-substantial	18	1.4	0.7 to 2.5	10	1.1	0.5 to 2.3
	Substantial	3	1.3	0.3 to 4.6	3	2.3	0.6 to 9.6
Formaldehyde	Any	13	0.9	0.5 to 1.8	10	1.2	0.5 to 2.5
Alkanes (C_5 to C_{17})	Any	33	0.9	0.6 to 1.5	25	1.3	0.7 to 2.3
	Non-substantial	15	1.2	0.7 to 2.2	14	1.5	0.7 to 3.1
	Substantial	18	0.7	0.4 to 1.3	11	1.1	0.5 to 2.3
Alkanes (C_{18+})	Any	29	0.8	0.5 to 1.2	21	1.0	0.6 to 1.8
Cleaning agents	Any	17	1.0	0.6 to 1.8	10	0.8	0.4 to 1.8

*Adjusted for age, respondent status, birthplace, educational level, beer consumption, spirits consumption, β-carotene index, cigarette-years, smoking patterns.
†This group comprises paints used on surfaces other than metal and varnishes used on surfaces other than wood.
PAHs=polycyclic aromatic hydrocarbons; n_{exp}=number of exposed cases.

Table 5 Adjusted OR (95% CI) between oesophageal cancer and exposure to selected substances, with three statistical models, by histological subtype, Montreal, 1979–85*

	All histological subtypes			*Squamous cell carcinoma*		
	n_{exp}†	*OR*	*95% CI*	n_{exp}	*OR*	*95% CI*
Model 1:						
Carbon black	9	1.7	0.8 to 3.8	8	2.9	1.2 to 7.1
Sulphuric acid	15	2.2	1.1 to 4.2	10	2.8	1.2 to 6.2
Model 2:						
Carbon black	9	1.9	0.8 to 4.7	8	2.6	1.0 to 7.0
Sulphuric acid	15	2.3	1.2 to 4.4	10	2.7	1.2 to 6.1
Toluene	13	0.8	0.4 to 1.6	12	1.2	0.5 to 2.7
Model 3:						
Carbon black	9	2.1	0.8 to 5.3	8	2.6	0.9 to 7.2
Sulphuric acid	15	2.7	1.3 to 5.5	10	3.0	1.2 to 7.2
Toluene	13	0.8	0.4 to 1.7	12	1.1	0.4 to 2.5
Chrysotile asbestos	18	1.4	0.7 to 2.7	14	1.7	0.8 to 3.6
Other paints and varnishes†	14	1.4	0.7 to 2.7	12	1.7	0.8 to 3.8
Iron compounds	18	0.6	0.3 to 1.1	15	0.7	0.3 to 1.7

*Adjusted for age, respondent status, birthplace, educational level, beer consumption, spirits consumption, β-carotene index, cigarette-years, smoking patterns.
†This group comprises paints used on surfaces other than metal and varnishes used on surfaces other than wood.
n_{exp}=Number of exposed cases.

broccoli, lettuce and endives, green beans and peas, brussels sprouts, tomato products, and apricots, peaches, plums and nectarines into seasonally adjusted median intake of β-carotene.[21] This combination of non-occupational factors provided the best fit for the data at hand.

Results

Descriptive characteristics of the cases of oesophageal cancer and control groups are presented in table 2. The cases had a lower educational level than the control subjects, were more likely to have had a proxy respondent complete their interview, were more likely to drink alcohol heavily, had a lower β-carotene index, had smoked more cigarettes in their lifetime, and were less likely to have stopped smoking or had stopped smoking only very recently. The sociodemographic variables were similar across the different control groups.

Table 3 shows the substances selected for study as well as the most common occupations in the Montreal case-control study which were allocated exposure to those substances. These are the occupations with the largest numbers of men exposed to this substance in the sample, and are not necessarily the occupations with the highest concentrations of exposure. Although most of the substances are self explanatory, two variables, mineral spirits and other paints and varnishes require clarification. Two types of mineral spirits were coded, early formulations (generally before 1970) which included benzene, toluene, and xylene, and later formulations which did not include these constituents. In our preliminary analyses, only exposure to the early formulation was associated with oesophageal cancer. Thus this one was selected for the present analysis; for simplicity, we labelled it as mineral spirits, but it should be noted that it refers to the earlier formulations. The grouping of other paints and varnishes comprises paints used on surfaces other than metal and varnishes used on surfaces other than wood. It should also be noted that the substances are not mutually

Table 6 Adjusted OR (95% CI) between oesophagus cancer and selected occupations and industries, by histological subtypes, Montreal, 1979–85*

		All histological subtypes (n=99)			*Squamous cell carcinoma (n=63)*		
Occupation or industry	*Duration (y)*	n_{exp}	*OR*	*95% CI*	n_{exp}	*OR*	*95% CI*
Occupations:							
Administrators and managers	Any	11	1.1	0.5 to 2.3	8	1.3	0.5 to 3.0
	<10	4	1.9	0.6 to 6.0	3	2.3	0.6 to 8.8
	⩾10	7	0.9	0.4 to 2.1	5	1.0	0.3 to 2.8
Salesmen	Any	21	0.9	0.5 to 1.6	15	1.1	0.6 to 2.1
Warehouse workers	Any	15	1.7	0.9 to 3.3	10	2.0	0.9 to 4.4
	<10	9	1.8	0.8 to 3.9	6	1.9	0.7 to 4.9
	⩾10	6	1.7	0.6 to 4.5	4	2.2	0.7 to 7.2
Clerks	Any	17	0.9	0.5 to 1.6	9	0.7	0.3 to 1.5
Police, guards, firefighters	Any	23	1.3	0.8 to 2.3	12	1.0	0.5 to 2.1
	<10	17	1.3	0.7 to 2.4	7	0.8	0.3 to 1.9
	⩾10	6	1.4	0.5 to 3.7	5	1.7	0.6 to 5.1
Construction workers	Any	17	0.9	0.5 to 1.6	12	0.9	0.5 to 1.9
Motor transport workers	Any	14	0.7	0.4 to 1.4	6	0.5	0.2 to 1.3
Food services workers	Any	10	1.7	0.8 to 3.7	5	1.1	0.4 to 3.2
	<10	3	1.1	0.3 to 3.9	1	0.6	0.1 to 4.5
	⩾10	7	2.3	0.9 to 6.0	4	1.6	0.5 to 5.5
Chefs and cooks	Any	7	1.7	0.7 to 4.1	3	0.9	0.3 to 3.5
	<10	3	1.7	0.5 to 6.4	1	1.1	0.1 to 8.5
	⩾10	4	1.6	0.5 to 5.5	2	0.9	0.2 to 4.7
Food processors	Any	6	0.6	0.3 to 1.5	2	0.3	0.1 to 1.2
Industries:							
Government	Any	12	1.0	0.5 to 2.0	8	1.1	0.5 to 2.6
Retail trades	Any	12	0.6	0.3 to 1.2	10	0.9	0.4 to 1.8
Wholesale trade	Any	11	0.9	0.4 to 1.8	8	1.1	0.5 to 2.5
Services to business	Any	11	1.6	0.7 to 3.3	5	1.1	0.4 to 3.0
	<10	7	1.7	0.7 to 4.4	2	0.8	0.2 to 3.6
	⩾10	4	1.3	0.4 to 4.3	3	1.4	0.4 to 5.8
Construction	Any	17	0.8	0.5 to 1.5	14	1.0	0.5 to 2.0
Defence services	Any	19	1.1	0.6 to 1.9	11	0.8	0.4 to 1.7
Accomodation and food	Any	12	1.7	0.8 to 3.4	7	1.5	0.6 to 3.8
	<10	5	1.5	0.5 to 4.2	2	1.0	0.2 to 4.7
	⩾10	7	1.9	0.7 to 4.8	5	1.9	0.6 to 5.8
Miscellaneous food	Any	4	2.1	0.7 to 6.4	4	3.7	1.1 to 11.9
Beverages	Any	5	1.2	0.4 to 3.4	3	1.1	0.3 to 4.0

*Adjusted for age, respondent status, birthplace, educational level, beer consumption, spirits consumption, β-carotene index, cigarette-years, smoking patterns.
n_{exp}=Number of exposed cases.

exclusive; for instance, there are some specific ones—for example, toluene—that are subsets of some general ones—for example, solvents.

There was little difference between relative risk estimates for occupational exposures based on the three control groups. Consequently, we only present the results based on the group of 1066 pooled controls.

SUBSTANCES

The odds ratios (ORs) for oesophageal cancer with exposure to the selected occupational agents are presented in table 4. Risk estimates are shown for all histological subtypes combined, as well as for squamous cell carcinomas only. Odds ratios are presented for any exposure and for those agents associated with an OR of $\geqslant 1.3$, for any and substantial exposure.

For the most part, ORs were higher for squamous cell carcinomas than for all oesophageal cancers combined. Where there were excess risks, it seemed that the excess was concentrated among the squamous cell carcinomas.

There was evidence of a twofold to threefold increase in risk of squamous cell carcinoma among subjects ever exposed to carbon black, chrysotile asbestos, and alumina. The ORs for any and substantial exposures to carbon black were significant and showed a dose-response pattern. The risks for exposure to cellulose, wood dust, and crystalline silica were not increased.

The risk estimates for squamous cell carcinoma among subjects exposed to liquids and vapours such as mineral spirits, toluene, synthetic adhesives, other paints and varnishes, and sulphuric acid ranged from 1.8 to 3.1. Exposure to the entire class of solvents conferred a 40% excess in risk. There was some evidence of increased risks with increasing exposure to toluene, sulphuric acid, and solvents, but only for sulphuric acid were ORs significantly increased with any and substantial exposure (based on all histological subtypes). Subjects exposed to lubricating oils and greases showed no increase in risk.

The gases and fumes considered for analysis included metal oxide fumes, nitrogen oxides, gasoline engine emissions, and carbon monoxide. There was little evidence of increased risks for these substances, except perhaps for metal oxide fumes.

Iron compounds and mild steel dust showed significant excesses in risk of squamous cell carcinoma in the any exposure subgroup. The ORs associated with exposure to the other metals under study showed little or no increase in risk.

None of the aromatic hydrocarbons analysed showed clear excesses in risk; only benzo(a)pyrene and PAHs from coal were marginally increased. Neither was there evidence of increased risks among subjects exposed to the other substances under study, including formaldehyde.

The results presented so far are based on analyses carried out on individual substances. As there was considerable overlap in occupational exposure patterns, it is quite likely that the results for the various substances are mutually confounded. In an attempt to correct for this, we developed three regression models incorporating multiple occupational substances. The first model included, along with the set of non-occupational variables, those two substances (carbon black and sulphuric acid) perceived to have the strongest association with oesophageal cancer, based on the presence of a dose-response trend and on the 95% confidence intervals (95% CIs) excluding one, for both any and substantial exposure, either for all oesophageal cancers combined or for squamous cell carcinomas. In the second model, we added toluene, which reached significance for any exposure only. The third model included three other substances that showed weaker evidence of an association—namely, asbestos, other paints and varnishes, and iron compounds. These were selected from the group of substances with 95% CIs including 0.9, but excluding highly correlated substances. Results from these models are presented in table 5. When carbon black and sulphuric acid were incorporated into the same model (model 1), the ORs for exposure to both substances remained high and reached significance. Addition of toluene (model 2) induced minimal changes for the first two substances but the apparent excess risk with exposure to toluene found in the single substance analyses practically disappeared. When substances with weaker evidence of an association were added to the model (model 3), the same patterns of risk remained for carbon black and sulphuric acid.

OCCUPATIONS AND INDUSTRIES

Table 6 presents the logistic regression results for the selected industries and occupations. Odds ratios are presented for any exposure to the occupation or industry of interest, as well as for two duration categories (<10 years, $\geqslant 10$ years) whenever the OR among those ever exposed was $\geqslant 1.3$. There were no occupations or industries with clear patterns of excess risks although the numbers were small and the statistical power low. The strongest indications were evident for warehouse workers, food services workers, and for workers from the miscellaneous food industry.

Discussion

This study is the first to examine many of these specific occupational exposures as possible risk factors for oesophageal cancer. Although the total number of cases we had access to were limited, the occupational circumstances retained for analysis had reasonable numbers of exposed cases. The present study benefited from reliable exposure information,[22] collected with a method that is recognised as the best approach for such study design.[23] Other advantages included the access to incident cases with confirmed histological profiles, access to different control groups, and the availability of information on important potential confounders. Specifically, unlike most occupational cohort studies, we had data and were able to

control for the effects of major potential confounders—for example, smoking, alcohol, and fruit and vegetables containing β-carotene. Unlike our preliminary report,[15] the present set of analyses focused on the subset of substances, occupations, and industries which were common and therefore provided more stable risk estimates.

SUBSTANCES

Most of the liquids and vapours analysed in this study were significantly associated with the risk of oesophageal cancer—for example, mineral spirits, toluene, synthetic adhesives, other paints and varnishes, and sulphuric acid. However, many of these exposures were highly correlated among each other.

Perhaps the most convincing evidence of an association with oesophageal cancer in this study is for sulphuric acid. This substance is used in the manufacture of fertilisers, rayon, and soap, and is also used in the pickling and cleaning of metals, as an electrolyte in batteries, and in the purification of petroleum products. It has been linked with lung and laryngeal cancers.[24] Nevertheless, the available evidence on oesophageal cancer is sparse. A retrospective cohort study of metal polishers and platers found an increased risk of oesophageal cancer based on nine deaths,[25] and an ecological study found an increased risk of oesophageal cancer in United States counties with metal electroplating industries.[26] However, a Swedish study which linked incident cases of oesophageal cancer between 1961 and 1979 with 1960 census data on occupation found no increased risk for work as a metal plater[11] and a Swiss study that used death certificate information on occupation found an increased risk of oesophageal cancer in foundry workers but not in other industries related to metal.[27] Pulp and paper workers may be exposed to several chemicals including sulphuric acid. A Canadian study suggested that these workers may have increased risks of cancer of the oesophagus.[28]

The group of synthetic adhesives includes all adhesives based on synthetic resins and rubbers—such as formaldehyde resins, epoxy resins, polyvinyl acetate resins, and hot melts. They are used in many industries, particularly the furniture and shoe industries. Two cohorts of shoe manufacturers showed no increase in risk of oesophageal cancer.[29] The Swedish and Swiss studies mentioned previously found no increased risk for work either in furniture manufacturers or shoe and leather workers.[11 27]

The main occupation groups exposed to other paints and varnishes were painters and carpenters. A wide range of chemicals are present in paints, including organic solvents and dye products. Workers from this study exposed to these substances had significantly increased risks but no dose-response trend emerged. Several studies document some excess risks of oesophageal cancer among painters,[30–33] but others provide no support for such an association.[11 27 34]

Our findings also provide support for an association between oesophageal cancer and carbon black. Workers exposed to this agent had significant excesses of oesophageal cancer as a whole (OR 2.1) and in particular of squamous cell carcinoma (OR 3.4), with evidence of a dose-response pattern. Carbon black is a dust containing mainly carbon with traces of polycyclic aromatic hydrocarbons and is used in industries producing rubber products and printing inks. It has been associated with lung cancer in this study population[35] as well as in others.[36] Several studies have noted excess risk of oesophageal cancer in the rubber industry[11 37–39] but the evidence is not entirely consistent.[40–43] Increased risks have also been reported in the printing industry.[15 44 45]

We found evidence of a significant twofold increase in risk of squamous cell carcinoma with exposure to chrysotile asbestos. There were too few subjects with substantial exposure to comment on the dose-response trend. Workers in occupations possibly entailing asbestos exposure such as insulation workers, plumbers, and carpenters have previously been reported to be at excess risk of oesophageal cancer.[15 27 46 47] In another study, there was no clear increase in risks among workers exposed to asbestos.[19]

Increased ORs were found for any exposure to iron compounds and mild steel dust. The numbers with substantial exposure were limited. A small increase in risk was suggested in a study of workers ever exposed to metal dust.[19] We found no higher risk with exposure to hexavalent chromium compounds. A modest increase in risk has been reported among workers exposed to chromium.[19] Some occupations possibly entailing exposure to metals such as sheet metal workers,[47] metal polishers and platers,[15 25] jewellery workers,[48] and foundry workers in the metal industry[27] have been associated with oesophageal cancer.

Alumina, a widely used abrasive, and abrasive dust are often found in the work environment of metal machinists, motor vehicle mechanics, and carpenters. Our data are suggestive of an excess risk with exposure to alumina.

We found no association between exposure to cellulose, wood dust or crystalline silica, and cancer of the oesophagus. A study assessing the role of silica dust found increased risks among exposed workers,[49] whereas another reported no excesses among those exposed to wood dust and quartz.[19]

Workers with any exposure to metal oxide fumes showed some excesses in risks, but these did not reach significance. There was little evidence in our data that exposures to nitrogen oxides, gasoline engine emissions, or carbon monoxide represent a risk for oesophageal cancer. A few studies evaluating the morbidity or mortality in occupational groups likely to be exposed to air pollutants generated by motor vehicles have found increased risks among urban bus drivers,[50] professional drivers,[51 52] and truck and tractor drivers.[53] In many studies, it was not possible to adjust for important covariates. One investigation suggests that workers exposed to combustion by products—for example, chimney sweeps, waste incinerator workers, gas workers, and bus garage

workers—may have increased risks of oesophageal cancer.[54]

Two types of polycyclic aromatic hydrocarbons showed some weak link with oesophageal cancer in this study—for example, benzo(a)pyrene and PAHs from coal. These findings concord with previous analyses of this data set.[55] A twofold increase in risk with exposure to PAHs was evident in a recent study although no dose-response pattern emerged.[19] Chimney soot contains carcinogens—such as PAHs—and increased risks have been reported in chimney sweeps.[56 57] Polycyclic aromatic hydrocarbons are present in the environment of asphalt workers and there is evidence of higher risks in this occupation group as well.[54]

Neither aliphatic aldehydes nor formaldehyde, an important constituent, showed clear increase in risks of oesophageal cancer. By contrast, one study found increased risks among workers exposed to formaldehyde.[19]

Finally, our data suggested no association with alkanes C_5-C_{17} (the major components of petroleum solvents and fuels—such as gasoline), with alkanes C_{18+} (used in petroleum jelly), or with cleaning agents that excluded organic solvents.

Workers in the dry cleaning industry are exposed to organic solvents—such as percholoethylene. Several studies have suggested that dry cleaning workers may have increased risks of oesophageal cancer.[58–61] In some of these, however, confounding by alcohol and smoking could not be ruled out. Increased risks have been reported among jewellery workers, which can also be exposed to solvents.[48] The paucity of study subjects who had worked in these industries precluded analyses of these occupational groups.

Because so few people were exposed, it proved difficult to disentangle the effects of the different substances under study. We attempted to clarify mutual confounding between occupational substances with three different regression models, firstly by incorporating substances with strong evidence only, then adding those with weaker evidence. All models were consistent with increased risks with exposure to sulphuric acid and carbon black.

OCCUPATIONS AND INDUSTRIES

Although we think that the most important results from this study are those based on specific substances, the job-title analyses enable us to compare our data with the available evidence, largely based on occupations. As occupations and industries were mutually exclusive, control for confounding involved adjusting for non-occupational factors only.

Administrators and managers in the short duration category showed some excess in risk but 95% CIs were wide. This agrees with findings of higher risks of cancer of the cardia and lower oesophagus among workers with administrative jobs.[62] However, we found no evidence of higher risks among salesmen, or in the retail or wholesale trades, as suggested previously.[11] At least one other study documents an excess risk in warehouse workers.[53]

Food services workers and workers in the miscellaneous food industry showed increased risks of oesophageal cancer in this study. There were also some indications of higher risks among chefs and cooks, and in the accommodation and food industry. Except for workers from the miscellaneous food industry, risks tended to be lower for squamous cell carcinoma than for all histological subtypes combined. Food processors and workers in the beverages industry had no apparent increase in risks but numbers were small. The available evidence for an excess risk among food and beverages workers is compelling. For instance, increased risks have been documented among workers in the food, beverages, and tobacco industries,[11] among workers in the hotel and restaurant industries,[11 12] among waiters, bartenders, and brewery workers,[11 63–68] among wine growers,[27] butchers,[11] and among workers in abattoirs and meatpacking plants.[69] Confounding by alcohol intake and smoking, two strong risk factors for oesophageal cancer, undoubtedly explains at least part of the increased risks in these occupation groups. We tried several combinations of these variables in our regression models and selected the one that fitted best the data at hand. Nevertheless, some residual confounding may remain.

There was no clear evidence of increased risks among policemen, guards, or firefighters, or in the defence services. No excess mortality from oesophageal cancer has been noted in one previous report.[70]

Workers in the construction industry had no excess risk in this study. Increased risks have been reported among woodworkers, carpenters, masons, and construction labourers.[27] Nevertheless, one study found no increased risks among workers exposed to wood dust.[19]

Farmers have been found to have a reduced risk of oesophageal cancer in some[11 71 72] but not all studies.[73] There were too few cases in the present study to carry out analyses on agricultural workers.

Few data have been collected to assess whether occupational agents induce histologically specific types of oesophageal cancer. One study which examined histological types by major industries and occupations[11] found significant excess risks in the sales and business industries only, and risks were slightly higher for squamous cell carcinoma than for adenocarcinoma. The present study found increased risks for exposure to several occupational circumstances for both all oesophageal cancers combined, and for squamous cell carcinomas, but risks were often higher for squamous cell carcinomas. One striking exception seems to be for workers in occupations related to food, for whom risks of squamous cell carcinoma tended to be lower.

Given a set of risk factors, the fraction of oesophageal cancer attributable to occupational exposures can be computed. Taking the two substances with the strongest evidence, sulphuric acid and carbon black, combining them into a single exposure variable, and using methods developed by Bruzzi *et al*,[74] we estimate that 6.7% (95%CI 2.8 to 9.0) of all

oesophageal cancers and 8.1% (95%CI 4.1 to 10.1) of squamous cell carcinomas were attributable to these two occupational exposures. These estimates are of course predicated on the as yet unproved hypothesis that these are true risk factors for oesophageal cancer.

In summary, our findings suggest an excess risk of oesophageal cancer, particularly squamous cell carcinoma, with exposure to carbon black and sulphuric acid. Other substances showed excess risks, but the evidence was more equivocal—namely chrysotile asbestos, alumina, mineral spirits, toluene, synthetic adhesives, other paints and varnishes, iron compounds, and mild steel dust. Because of the overlap between many of these occupational exposures and the inherent difficulty in disentangling their effects, apparent increased risks related to one substance may be an indication of risks related to one of the others reported here, or indeed to another substance that was not assessed in this study. Increased risks were apparent for warehouse workers, food services workers, and workers from the miscellaneous food industry. Many of these associations have never been examined and warrant further investigation.

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